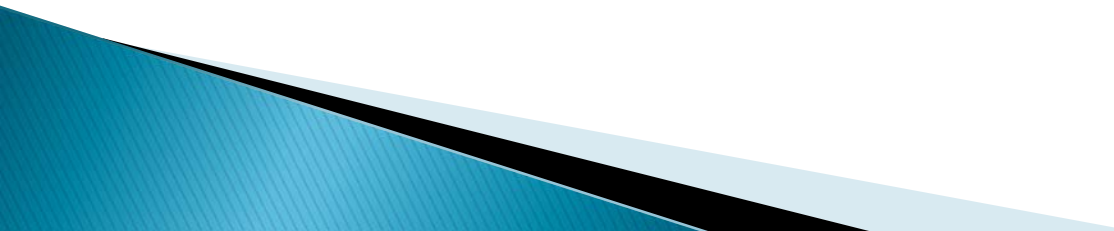


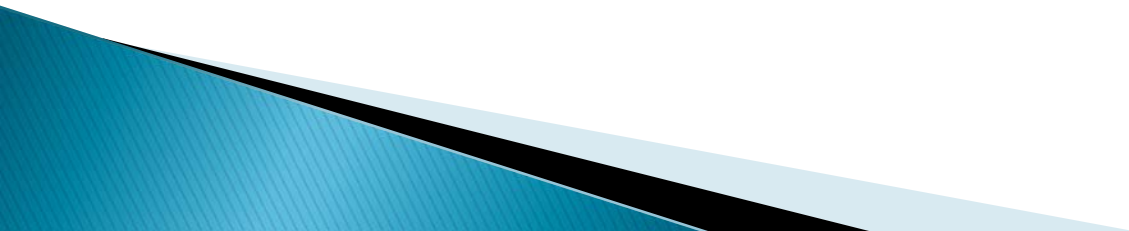
# HIV and Cancer

Noon Conference  
June 10, 2010  
Chris Farnitano, MD

# Learning Objectives

- ▶ By the end of this presentation participants are expected to:
  - ▶ Know which cancers are AIDS-defining illnesses
  - ▶ Understand that there is an increased prevalence of other types of cancer in HIV-infected individuals
  - ▶ Understand the rationale for more aggressive guidelines for initiating anti-HIV therapy
  - ▶ Be familiar with arguments for and against anal cancer screening
  - ▶ Understand how to collect an anal pap specimen
- 

# Forms

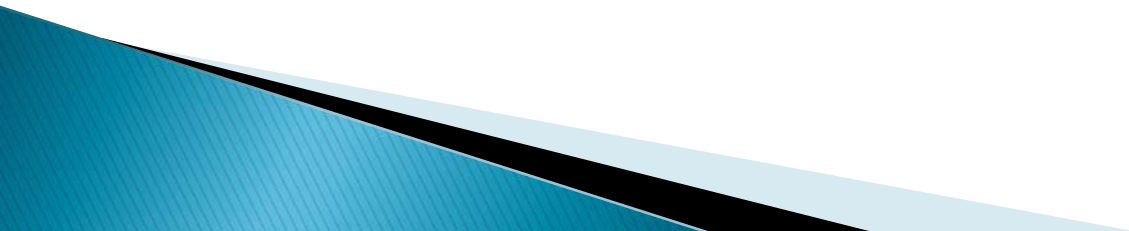


# HIV and Cancer Deaths

## PHC ID clinic experience

- ▶ 2004: 1 / 6 deaths due to cancer (small cell lung)
- ▶ 2005: 1 / 3 (small cell lung)
- ▶ 2006: 0 / 4
- ▶ 2007: 1 / 3 (prostate)
- ▶ 2008: 1 / 1 (laryngeal)
- ▶ 2009: 0 / 1
- ▶ 2010: 0 / 1
- ▶ Total: 4 / 19 deaths from cancer at PHC = 21%
- ▶ In France 34% of all deaths in HIV+ in 2005 were from cancer, up from 29% in 2000

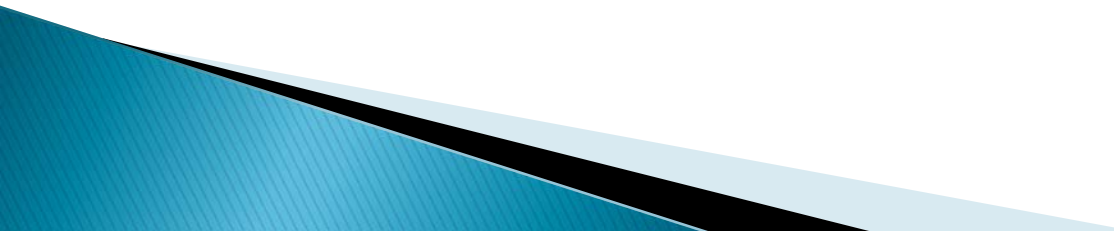
# What are the AIDS–Defining Malignancies?



# AIDS Defining Cancers

- ▶ Kaposi's Sarcoma
  - ▶ Non-Hodgkin's Lymphoma
  - ▶ Invasive Cervical Cancer
- 

# Kaposi's Sarcoma

- ▶ 100–300x more likely in HIV pos
  - ▶ HIV-related KS associated with Human Herpes Virus 8 (HHV-8)
  - ▶ More common with lower T Cells
  - ▶ Was the AIDS defining illness in 30% of individuals in 1980s
  - ▶ Now uncommon with use of Anti-Retroviral Therapy
- 



# Kaposi's Sarcoma

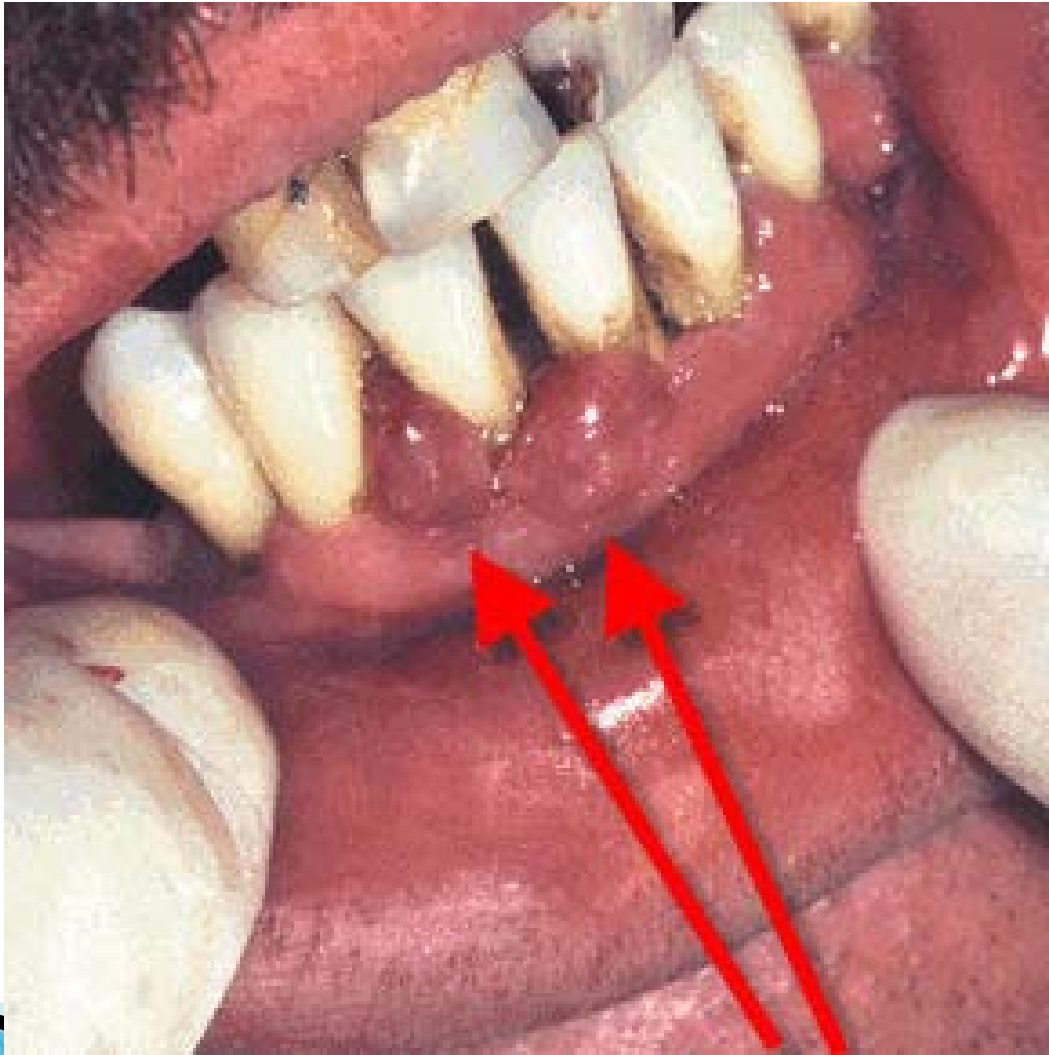




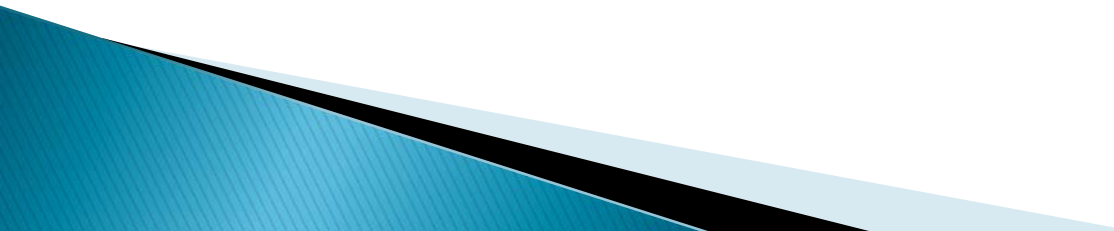
# Non-Hogkins' Lymphoma

- ▶ 40–400x more likely in HIV pos
- ▶ More often high grade in HIV pos
- ▶ Increased frequency with declining T Cells
  - Especially primary CNS lymphoma (PCNSL)
- ▶ Incidence of lymphoma decreased by over 50% in patients on antivirals

# Non-Hogkins' Lymphoma



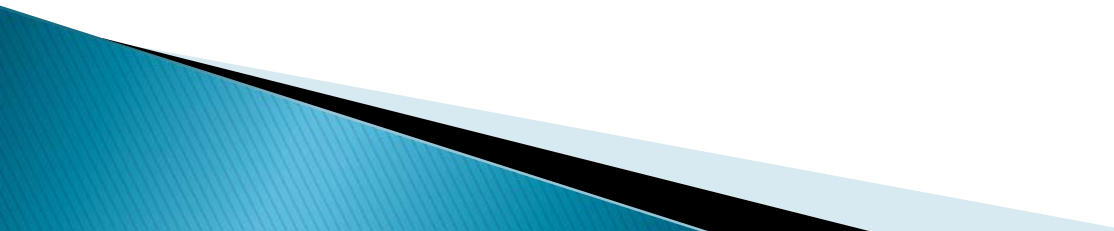
# Invasive Cervical Cancer

- ▶ 10x as common in HIV pos women
  - ▶ HIV pos women more likely to acquire HPV infection
  - ▶ HIV pos women with dysplasia more likely to progress
  - ▶ Not as clear a connection between low T cells and increased frequency of cervical cancer
  - ▶ Data conflicting on benefit of HAART on disease acquisition or progression
- 

# Invasive Cervical Cancer



# AIDS–Associated malignancies

- ▶ Overall a 2–3 fold increased rate of these cancers in HIV pos vs. HIV neg
  - ▶ Lung Cancer and Hogkins lymphoma most common
  - ▶ Liver cancer rates 7 times higher in HIV+
- 

# AIDS–Associated malignancies

- ▶ Overall a 2–3 fold increased rate of these cancers in HIV pos vs. HIV neg
- ▶ Which cancers are HIV patients at increased risk of?

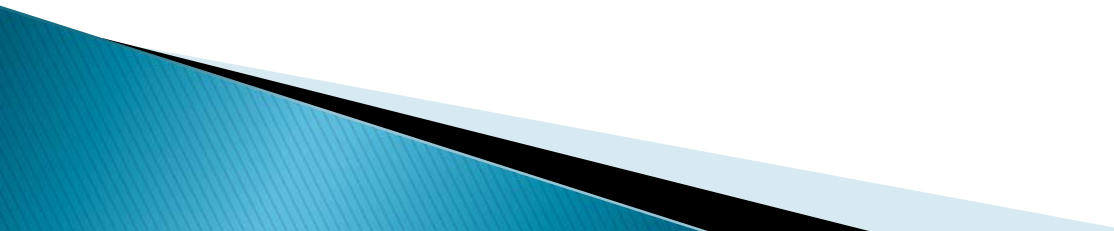
# AIDS–Associated malignancies

## Incidence rates vs. HIV neg

- ▶ Hodgkin's Lymphoma: 18x increase
- ▶ Anal Cancer 30–60x increase
- ▶ Lung Cancer 2.5–7.5x increase
  - Rising rates as HIV population survives longer, ages
- ▶ Testicular Cancer 1.4–8.2x increase
- ▶ Head and Neck Squamous Cell Ca 2x increase



# Other malignancies with slight increase in incidence for HIV pos individuals

- ▶ Leukemia            pharynx            pancreas
  - ▶ Esophagus           brain            multiple myeloma
  - ▶ Melanoma           lip            kidney
  - ▶ Penile            tongue            colorectal
  - ▶ Vulva/vagina    stomach            angiosarcoma
  - ▶ Larynx            heart            leiomyosarcoma
  - ▶ **NOT Breast or Prostate**
- 

# New guidelines emphasize early treatment

- ▶ Previous guidelines:
- ▶ CDC 12/1/07:
  - “therapy should be initiated in patients...with a CD4 cell count <350”

# New guidelines emphasize early treatment

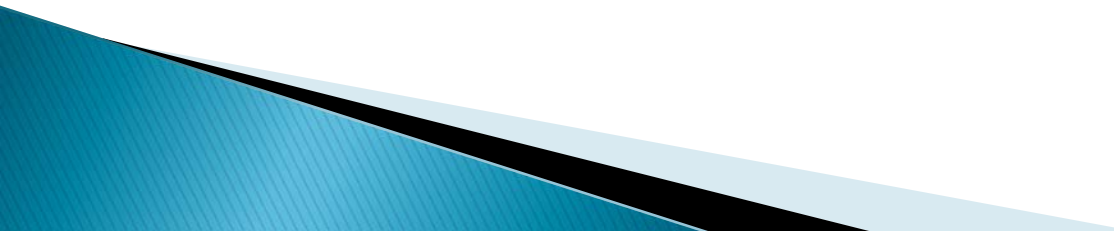
- ▶ When to Start: 2009 DHHS Guidelines
- ▶ CD4 Count Recommendations
  - ▶ • CD4 count  $<350$  cells/mm<sup>3</sup>
  - ▶ • CD4 count 350 – 500 cells/mm<sup>3</sup> \*
  - ▶ • CD4 count  $>500$  cells/mm<sup>3</sup> †
  - ▶ • • DHHS. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. December 1, 2009; 1–161.
- ▶ \* 55% of committee members favored strong recommendation; 45% favored moderate recommendation
- ▶ † 50% of committee members favored ART initiation; 50% view treatment as optional in this setting

# Why the guidelines change?

## ▶ IAS–USA:

- “at high CD4 counts, uncontrolled HIV replication and immune suppression are strongly associated with development of diseases not traditionally associated with HIV infection, such as non–AIDS cancer. . .and end–organ damage, including cardiovascular, hepatic, and renal dysfunction.”

# Increased risk of non-AIDS defining cancer with lower T cell counts

- ▶ Those with T cells between 400–699 at higher risk of cancer than those with T cells  $>700$
  - ▶ Three-fold higher risk with T cells 201–399
  - ▶ Highest risk at T cells  $<200$
- 

# NA-ACCORD analysis

- ▶ Analysis of 17,517 asymptomatic HIV+ US and Canada
  - Antiretroviral naive
  - Compare mortality between those starting ART at:
    - <350 (deferred) vs
    - CD4 350-500
    - CD4 >500
  - **Kitahata, NEJM, 2009**

# NA-ACCORD analysis:

## Retrospective case control study

- ▶ Higher risk of death in deferred ART group vs >350 CD4
  - CD4 <350 vs 350-500 N=8362
    - Relative risk 1.69 (95% CI 1.26-2.26) of death
  - CD4 <500 vs >500 N=9155
    - Relative risk 1.94 (95% CI 1.37-2.79) of death
  - Other predictors of mortality: older age, injection drug use and HCV



# Anal Dysplasia

- 60x increase in incidence of anal cancer in HIV pos men who have sex with men (MSM)
- HIV+ MSM anal cancer rates 5X higher than HIV–MSM

# Anal Dysplasia: Anal sex not the only risk factor

- Increased rates in HIV+ heterosexual IVDUs
- 76% HIV+ women test positive for anal HPV DNA
- 36% of HIV+ with cervical dysplasia or penile warts who had never been on receiving end of anal sex have anal dysplasia

# Anal Dysplasia

- Incidence highest in those with lowest T cells
- More progression with low T cells
- More regression with high T cells
- But: no clear benefit of HAART on incidence
  - Rates have increased since HAART introduced
  - Likely due to patients living longer with HIV

# Appearance of anal cancer



**Figure 1.** Perianal area: preoperative appearance.

# Treatment of Invasive Anal Cancer

- ▶ Radiation
  - ▶ Chemotherapy
  - ▶ Radical Resection
- 

Kevin Winter



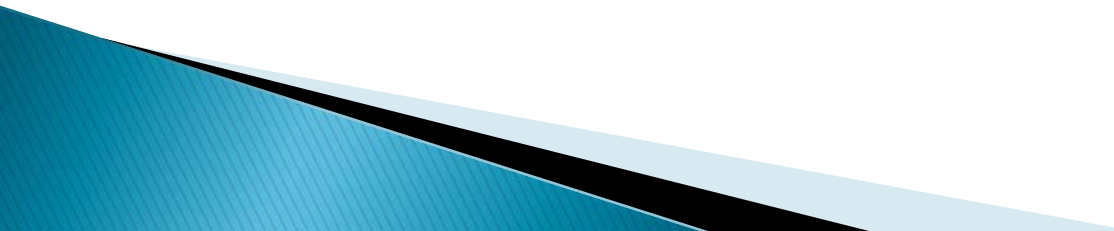
## **Farrah Fawcett: Anal Cancer**

**The former  
'Charlie's Angel'  
star battles a  
disease that's rare  
but on the rise.**

**By Sarah Kliff | Newsweek Web  
Exclusive Nov 14, 2007 | Updated:  
6:35 p.m. ET Nov 14, 2007**

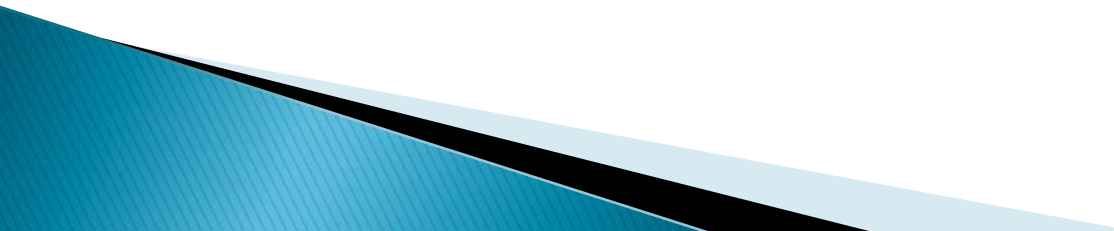
Exclu

# 5-year survival rates of Invasive Anal Cancer

- ▶ Localized: 80.6%
  - ▶ Regional mets: 61.1%
  - ▶ Distant mets 20.9%
- 



# Treatment of Anal Dysplasia

- ▶ Focus is on high grade dysplasia
  - ▶ Optimal treatment not defined
  - ▶ Options:
    - 80% Trichloroacetic acid
    - Liquid Nitrogen
    - Infrared Laser
    - Podophyllotoxin
    - Imiquimod
    - Surgical excision
    - Electrocautery (hyfrecator)
- 

# Treatment of Anal Dysplasia

- ▶ Options for low grade dysplasia:
  - Watchful waiting
  - Topical treatment

# Anal Pap Smears

- ▶ Arguments for screening:
  - High risk population has been identified
  - High disease burden: Anal cancer now more common in MSM than cervical cancer in women, rates continue to increase
  - Treatment of HGSIL much less morbidity than treatment of invasive anal CA

# Anal Pap Smears

- ▶ Arguments for screening:
  - Anal paps reliably detect anal dysplasia
  - Anal dysplasia a clear precursor for anal cancer
  - Treating anal dysplasia clearly decreases risk of invasive anal cancer

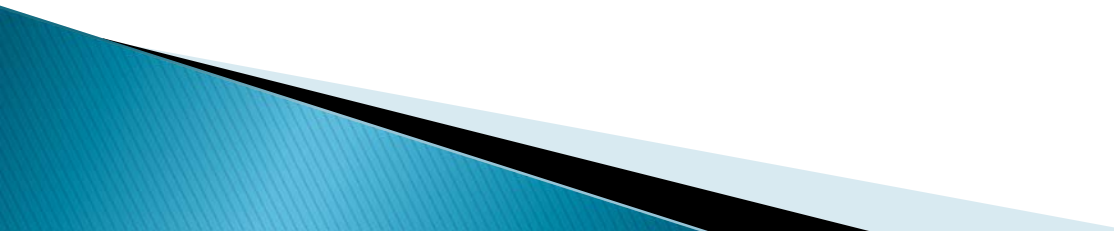
# Anal Pap Smears

- ▶ Arguments for screening:
  - Screening likely to be cost effective:
    - 1999 Cost/benefit analysis on hypothetical cohort of HIV+ men screened with yearly anal paps:
    - Cost of \$16,000 per quality adjusted life year gained
    - TMP/SMX for PCP prophylaxis costs \$13,000 for QALY
    - As incidence increases, Cost/benefit analysis should become even more favorable.

# Anal Pap Smears

- ▶ Arguments for screening:
- ▶ Some expert consensus panels now recommend it:
  - **New York State Department of Health Guidelines on HIV care:**
  - Clinicians should obtain anal cytology at baseline and annually in the following HIV-infected populations:
    - \* Men who have sex with men
    - \* Any patient with a history of anogenital condylomas
    - \* Women with abnormal cervical and/or vulvar histology

# Anal Pap Smears

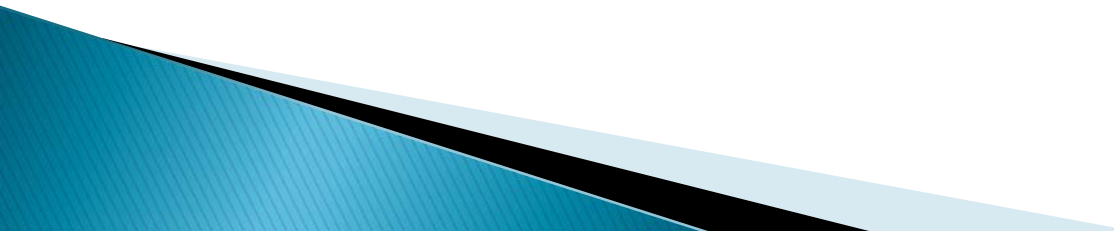
- ▶ Arguments against screening:
  - ▶ CDC states evidence insufficient to recommend routine anal pap smears
  - ▶ Lack of prospective studies on screened vs. unscreened population to show decrease in mortality with screening
- 



# Anal paps now routine part of primary HIV care

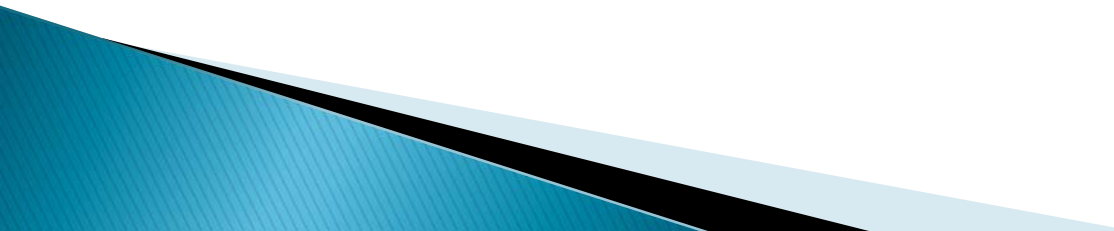
- ▶ At CCHS, most HIV clinicians routinely perform yearly anal paps in HIV+, especially MSM (but there is debate and doubt)
- ▶ 60 anal paps performed in 1<sup>st</sup> 6 months of 2008 at CCHS:
  - 35% normal
  - 15% unsatisfactory
  - 30% ASCUS
  - 17% LGSIL
  - 3% HGSIL

# Anal Paps, Who to screen?

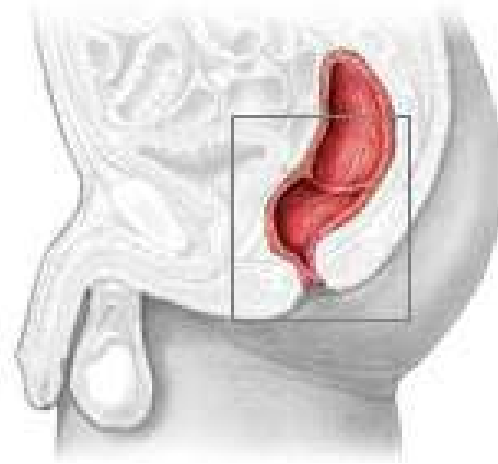
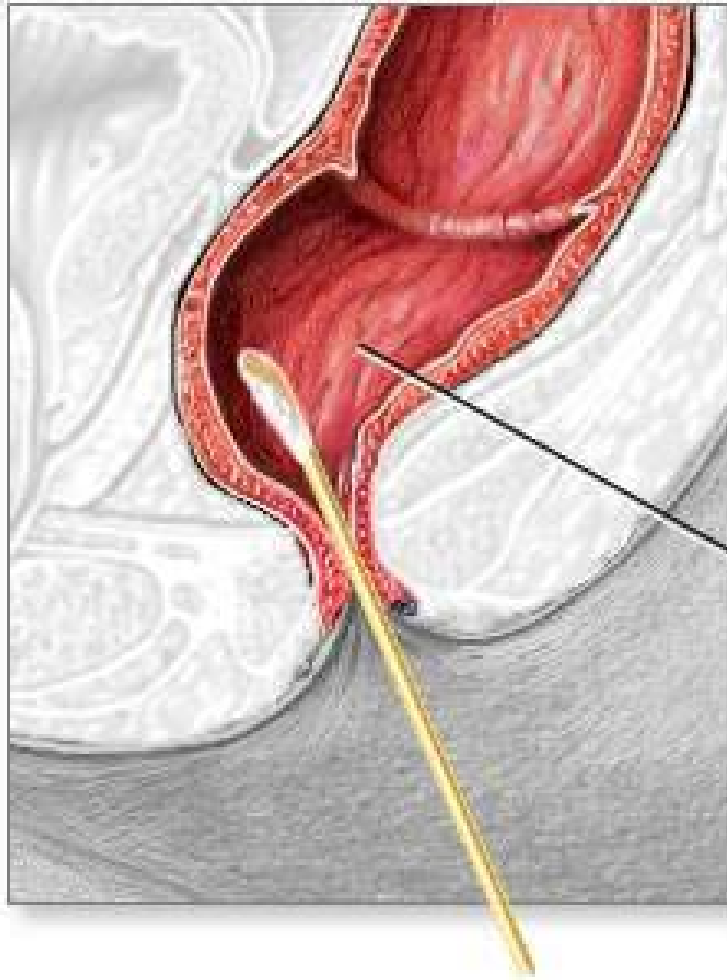
- ▶ MSM
  - ▶ HIV+ women
  - ▶ HIV+ men
  - ▶ Women with Hx of Cervical or Vulvar high grade dysplasia
  - ▶ Men and women with Hx of peri-anal condyloma
  - ▶ How often to screen? Q1,2 or 3 years?
  - ▶ When to stop screening?
- 

# How to Collect

## ▶ Standard Technique:

- Moisten Dacron or polyester swab with tap water
  - Insert swab 3–6 cm into anal canal until firm resistance is noted, rotate while inserting
  - Rotate swab and withdraw in a tight spiral motion over 15–20 seconds
- 

# How to Collect



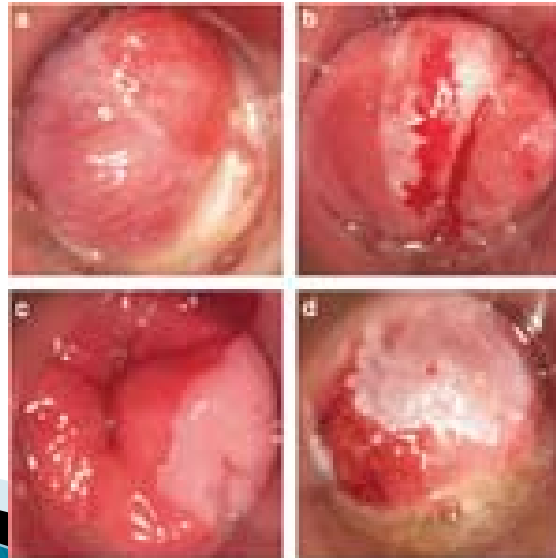
Rectum

# How to Collect

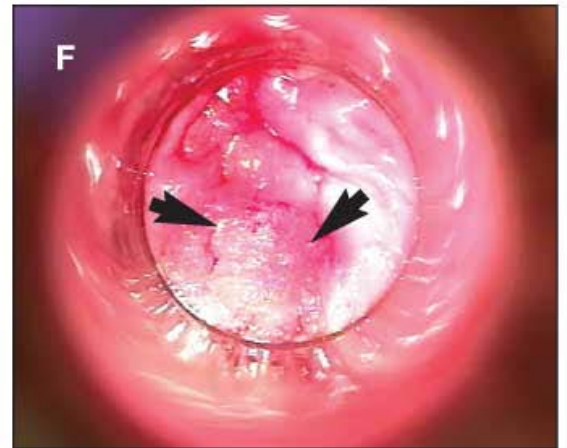
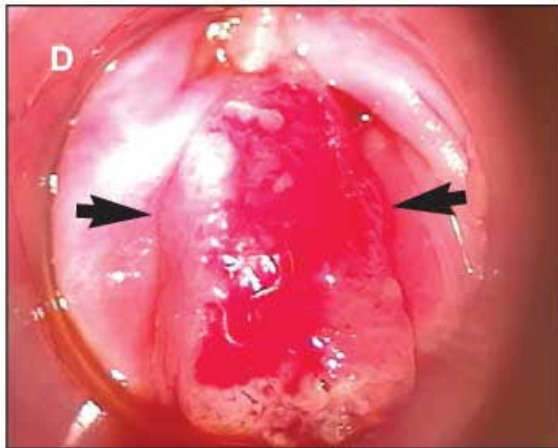
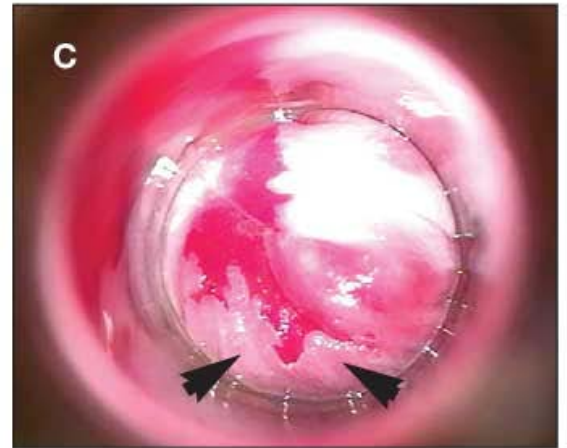
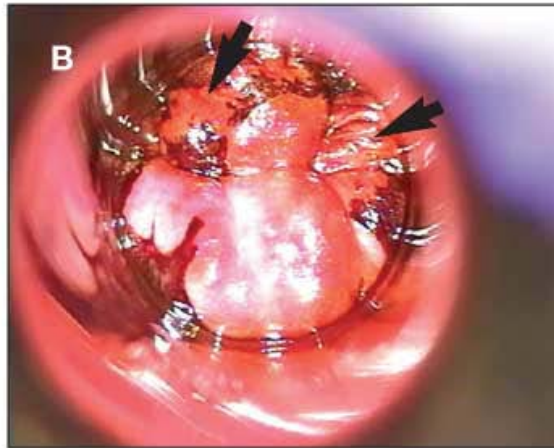
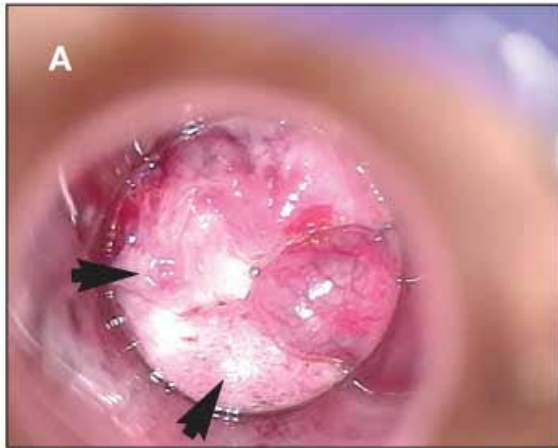
- ▶ Standard Technique:
  - Smear on glass slide or swish for 60 seconds and break off into liquid pap media.
  - Perform digital rectal exam after the anal pap to palpate for masses

# Management of Abnormal Anal Pap Smears

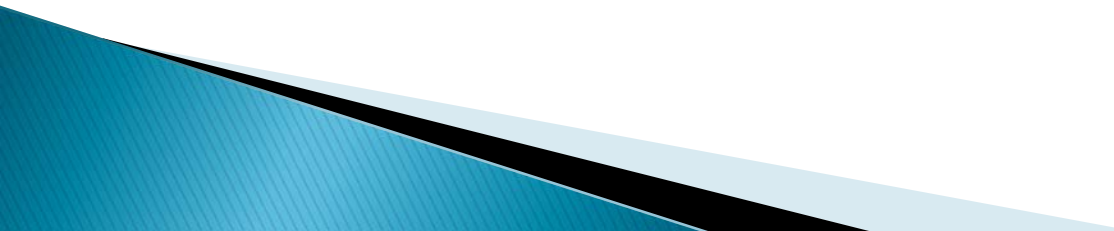
- ▶ Refer all ASCUS, LGSIL and HGSIL for high resolution anoscopy (HRA)
- ▶ Pap is sensitive for dysplasia but not specific for degree of dysplasia
- ▶ HRA similar to colposcopy: Using vinegar solution to identify acetowhite epithelium for biopsy



# High Resolution Anoscopy



# Where to refer patients for HRA:

- ▶ All patients:
  - ▶ UCSF Anoscopy clinic (at Mt. Zion campus):
    - Dr. Joel Palefsky, director
    - Phone: 415-353-4298
    - Fax: 415-476-5417
- 

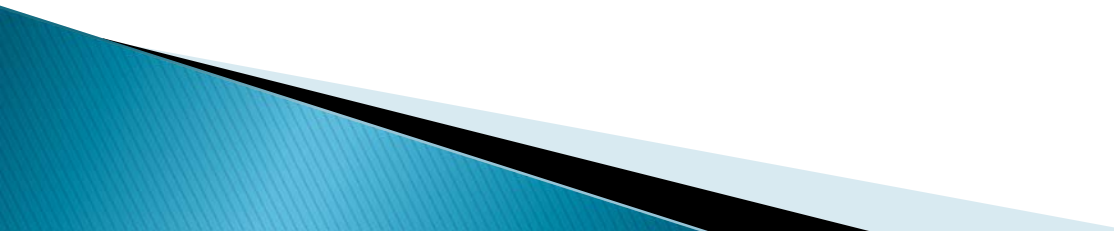


# Where to refer patients for HRA:

- ▶ The future:
- ▶ High Resolution Anoscopy clinic at CCHS?

Questions?

# Learning Objectives

- ▶ By the end of this presentation participants are expected to:
  - ▶ Know which cancers are AIDS–defining illnesses
  - ▶ Understand that there is an increased prevalence of other types of cancer in HIV–infected individuals
  - ▶ Understand the rationale for more aggressive guidelines for initiating anti–HIV therapy
  - ▶ Be familiar with arguments for and against anal cancer screening
  - ▶ Understand how to collect an anal pap specimen
- 

# Forms

